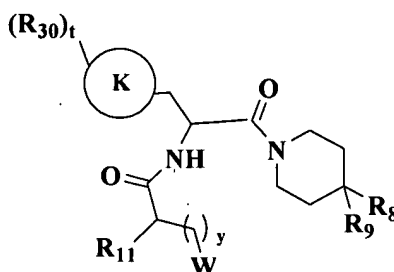


AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1. (Currently Amended) A compound according to the formula



or a pharmaceutically-acceptable salt or hydrate thereof,  
in which,

K is aryl or heteroaryl;

R<sub>8</sub> and R<sub>9</sub> are independently alkyl substituted with heteroaryl, cycloalkyl, aryl, and, -C(=O)R<sub>13</sub>,  
~~where one of R<sub>8</sub> and R<sub>9</sub> is alkyl substituted with heteroaryl and the other is cycloalkyl, or~~

~~where one of R<sub>8</sub> and R<sub>9</sub> is aryl and the other is~~  $\text{—}\overset{\text{O}}{\parallel}\text{C—alkyl};$

R<sub>11</sub> and R<sub>12</sub> are is selected from hydrogen, alkyl, halogen, hydroxy, hydroxyalkyl, haloalkyl, amino, aminoalkyl, alkylamino, arylalkyl, cycloalkylalkyl, heteroarylalkyl, aryl, and cycloalkyl, and where y is at least 1, then R<sub>11</sub> and R<sub>12</sub> may be heterocyclo or heterocycloalkyl;

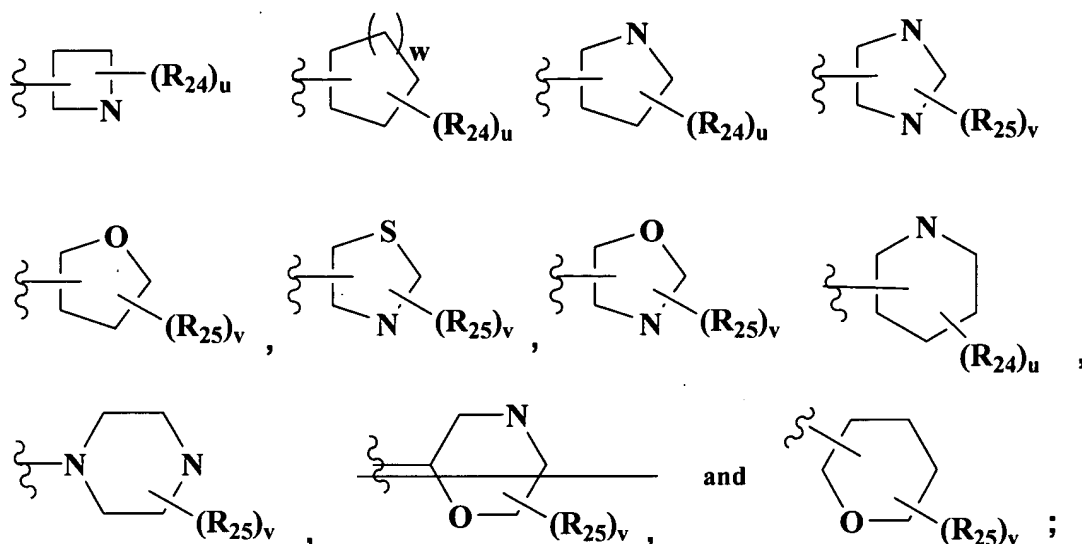
R<sub>13</sub> is alkyl;

W is selected from:

- 1) -NR<sub>16</sub>R<sub>17</sub>, -NR<sub>16</sub>C(=O)R<sub>22</sub>, -NR<sub>16</sub>CO<sub>2</sub>R<sub>22</sub>, -OR<sub>23</sub>, amidino, and guanidino;
- 2) heteroaryl or heterocyclo groups selected from pyrrolyl, furyl, thienyl, imidazolyl, pyrazolyl, isoxazolyl, thiazolyl, isothiazolyl, 3-azaisothiazolyl, pyridyl, pyrazinyl, pyridazinyl, 1,2-dihydropyridazinyl, and pyranlyl, wherein said heteroaryl and

heterocyclo groups may be substituted or unsubstituted and may have an optionally-substituted carbocyclic, heterocyclic or heteraryl ring fused thereto; or

3) a ring selected from:



$R_{16}$  and  $R_{17}$  are selected from hydrogen, alkyl and substituted alkyl;

$R_{18}$ ,  $R_{19}$  and  $R_{21}$  are independently hydrogen or  $C_{1-6}$ alkyl optionally substituted with halogen;

$R_{20}$  is  $C_{1-6}$ alkyl, aryl, or heteroaryl;

$R_{22}$  and  $R_{23}$  are independently selected from hydrogen, alkyl, substituted alkyl, aryl, heteroaryl, cycloalkyl, and heterocyclo;

$R_{24}$  and  $R_{25}$  at each occurrence are attached to any available carbon or nitrogen atom of W and at each occurrence are selected from hydrogen,  $C_{1-6}$ alkyl, halogen, substituted  $C_{1-6}$ alkyl, amino, alkylamino, cyano, nitro, trifluoromethoxy,  $-C(=O)R_{26}$ ,  $-CO_2R_{26}$ ,  $-SO_2R_{26}$ ,  $-OR_{26}$ , aryl, heteroaryl, heterocyclo, and cycloalkyl, and/or two  $R_{25}$  attached to two adjacent carbon atoms or adjacent carbon and nitrogen or carbon atoms may join to form a fused optionally-substituted heteroaryl, heterocyclo or cycloalkyl ring, and/or two  $R_{24}$  or two  $R_{25}$  when attached to the same carbon atom may form keto ( $=O$ );

$R_{26}$  is hydrogen, alkyl, substituted alkyl, aryl, heterocyclo, cycloalkyl, or heteroaryl, except when joined to a sulphonyl group as in  $SO_2R_{26}$ , then  $R_{26}$  is not hydrogen;

$R_{30}$  is attached to any available carbon or nitrogen atom of K and is selected from  $C_{1-4}$ alkyl, hydroxy, alkoxy, halogen, nitro, cyano, amino, alkylamino, phenyl, and  $-C(=O)$ phenyl; and

$k$  and  $m$  are independently 0, 1, 2 or 3;

$p$  is 1, 2, or 3;

$t$  is 0, 1 or 2.

$u$  and  $v$  are 0, 1, 2, or 3;

$w$  is 0, 1, or 2;

$y$  is 0, 1, 2, 3, or 4; and

$z$  is 0, 1 or 2.

Claim 2. (Cancelled).

Claim 3. (Previously Presented) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate thereof,

in which:

W is  $-NR_{16}R_{17}$ ,  $-NHC(=O)R_{22}$ ,  $-NHCO_2$ alkyl,  $OR_{23}$ , or azetidiny;

$R_{16}$  and  $R_{17}$  are independently selected from hydrogen,  $C_{1-8}$ alkyl, and  $(CH_2)_q$ -J, wherein J is selected from naphthyl, furanyl, indolyl, imidazolyl, pyrimidinyl, benzothienyl, pyridinyl, pyrrolyl, pyrrolidinyl, thienyl, and  $C_{3-7}$ cycloalkyl, wherein the alkyl, alkylene, and/or J groups of  $R_{16}$  and/or  $R_{17}$  are optionally substituted with up to three  $R_{32}$ ;

$R_{22}$  is selected from  $C_{1-6}$ alkyl, trifluoromethyl, alkoxyalkyl, furylalkyl, alkylaminoethyl, phenyl, pyrrolylalkyl, piperidinyl, and piperidinylalkyl, wherein  $R_{22}$  in turn is optionally substituted with one to two  $C_{1-4}$ alkyl and/or  $-CO_2(C_{1-4}$ alkyl);

$R_{23}$  is hydrogen or phenyl;

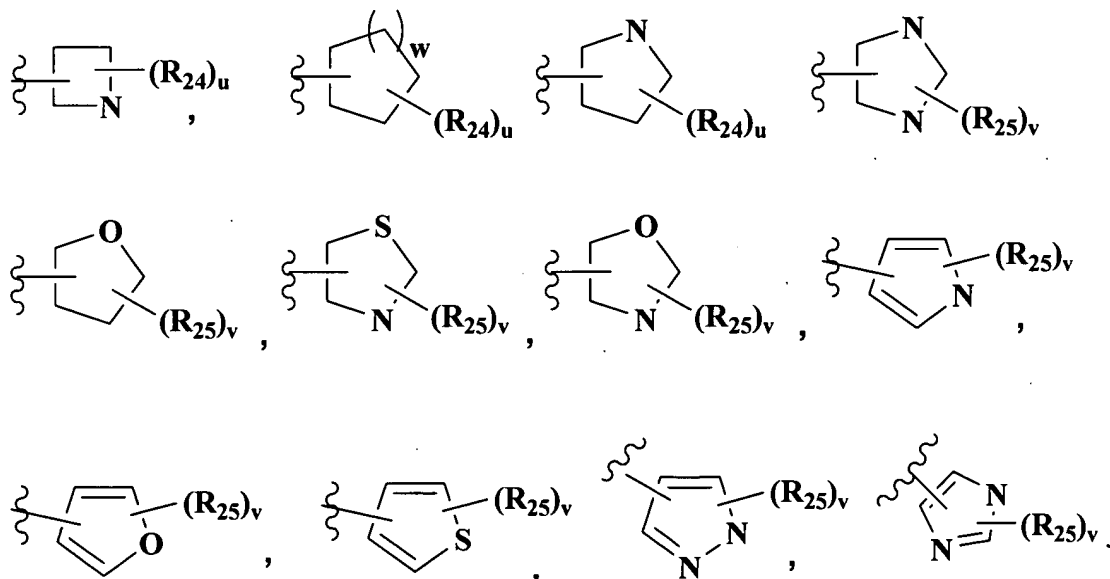
$R_{32}$  is selected from  $C_{1-6}$ alkyl, hydroxy,  $C_{1-4}$ alkoxy, amino,  $C_{1-4}$ alkylamino, amino $C_{1-4}$ alkyl, trifluoromethyl, halogen, phenyl, benzyl, phenyloxy, benzyloxy,  $-C(=O)(CH_2)NH_2$ ,  $-CO_2(C_{1-4}alkyl)$ ,  $-SO_2(C_{1-4}alkyl)$ , tetrazolyl, piperidiny, pyridinyl, and indolyl, wherein when  $R_{32}$  is a ring, said ring in turn is optionally substituted with one to two  $C_{1-4}$ alkyl, hydroxy, methoxy, and/or halogen; and

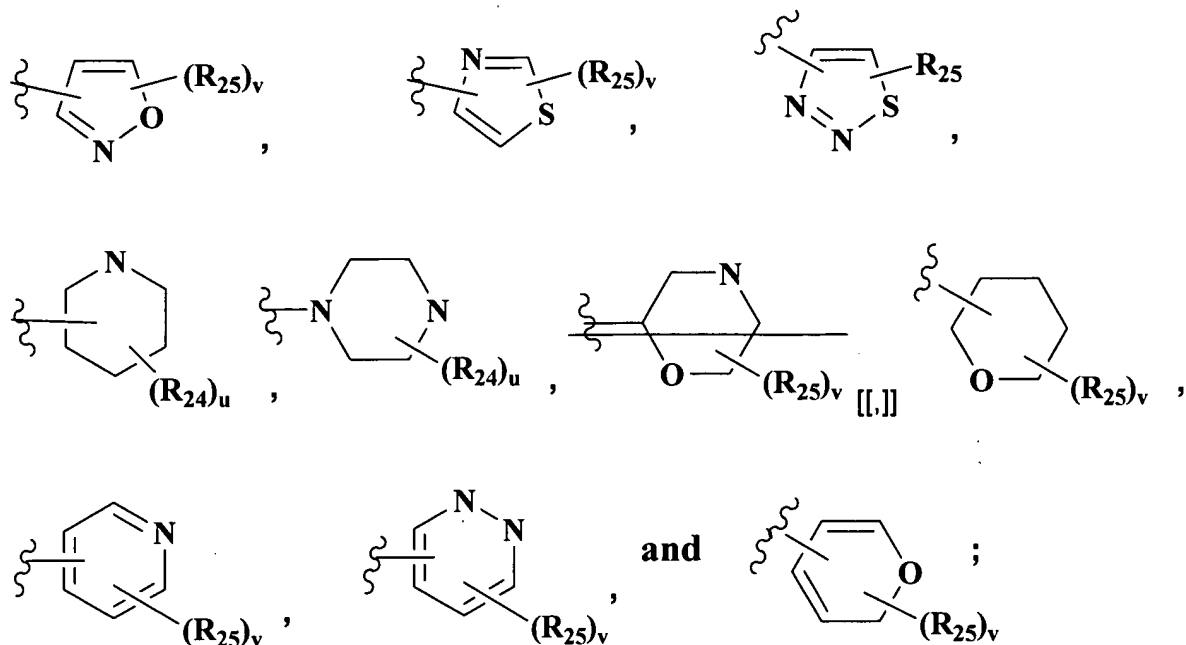
$q$  is 0, 1, 2 or 3.

Claim 4. (Currently Amended) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate thereof,

in which

W is a ring selected from:





$R_{24}$  is selected from keto ( $=O$ ),  $C_{1-6}$ alkyl, halogen, amino, aminoalkyl, alkylamino, hydroxy,  $C_{1-4}$ alkoxy, hydroxy $C_{1-4}$ alkyl,  $-C(=O)$ alkyl,  $-C(=O)$ aminoalkyl,  $-C(=O)$ phenyl,  $-C(=O)$ benzyl,  $-CO_2$ alkyl,  $-CO_2$ phenyl,  $-CO_2$ benzyl,  $-SO_2$ alkyl,  $-SO_2$ aminoalkyl,  $-SO_2$ phenyl,  $-SO_2$ benzyl, phenyl, benzyl, phenyloxy, benzyloxy, pyrrolyl, pyrazolyl, piperidinyl, pyridinyl, pyrimidinyl, and tetrazolyl, and each  $R_{24}$  in turn is optionally substituted with one to two  $R_{31}$ ;

$R_{25}$  at each occurrence is attached to any available carbon or nitrogen atom of W and is selected from  $C_{1-6}$ alkyl, halogen, amino, aminoalkyl, alkylamino, hydroxy,  $C_{1-4}$ alkoxy, hydroxy $C_{1-4}$ alkyl,  $-C(=O)$ alkyl,  $-C(=O)$ aminoalkyl,  $-C(=O)$ phenyl,  $-C(=O)$ benzyl,  $-CO_2$ alkyl,  $-CO_2$ phenyl,  $-CO_2$ benzyl,  $-SO_2$ alkyl,  $-SO_2$ aminoalkyl,  $-SO_2$ phenyl,  $-SO_2$ benzyl, phenyl, benzyl, phenyloxy, benzyloxy, pyrrolyl, pyrazolyl, piperidinyl, pyridinyl, pyrimidinyl, and tetrazolyl, and/or two  $R_{25}$  when attached to adjacent carbon atoms may be taken together to form a fused benzo or pyrazolyl ring, and/or two  $R_{25}$  when attached to the same carbon atom (in the case of a non-aromatic ring) may form keto ( $=O$ ), and each  $R_{25}$  in turn is optionally substituted with up to two  $R_{31}$ ;

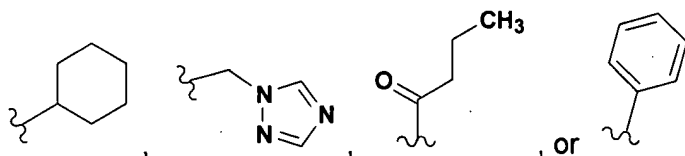
$R_{31}$  is selected from halogen, trifluoromethyl,  $C_{1-4}$ alkyl, hydroxy, and  $C_{1-4}$ alkoxy;

w is selected from 0, 1, or 2; and

$u$  and  $v$  are selected from 0, 1, and 2.

Claim 5. (Cancelled).

Claim 6. (Previously Presented) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate thereof, in which  $R_8$  and  $R_9$  are independently selected from



Claim 7. (Currently Amended) A compound according to claim 1 or a pharmaceutically-acceptable salt or hydrate or prodrug thereof, in which

$R_{11}$  is at each occasion independently selected from:

- a) hydrogen,
- b)  $C_{1-6}$ alkyl,
- c)  $C_{1-6}$ alkyl substituted with up to two of hydroxy, alkoxy, amino, alkylamino, imidazolyl, pyrazolyl, phenyl, naphthyl, pyridinyl, indolyl, pyrimidyl, furyl, thiazolyl, and thienyl, wherein said ringed substituents in turn are optionally substituted with one to three  $R_{33}$  and/or have a benzene ring fused thereto optionally substituted with one to two  $R_{33}$ ;
- d)  $C_{3-7}$ cycloalkyl optionally substituted with up to two  $R_{33}$  and/or having a benzene ring fused thereto, wherein said fused benzene ring is optionally substituted with up to two  $R_{33}$ ;
- e) phenyl optionally substituted with up to three  $R_{33}$ ;
- f) where  $y$  is at least one,  $R_{11}$  and  $R_{42}$  may also be selected from piperidinyl, pyrrolidinyl, piperidinylalkyl, and pyrrolidinylalkyl, in turn optionally substituted with up to three  $R_{33}$ ; or

ii) ~~alternatively, one of  $R_{11}$  and one of  $R_{12}$  attached to the same carbon atom may be taken together to form a spirocycloalkyl ring;~~

$R_{33}$  is selected from  $C_{1-6}$ alkyl, hydroxy,  $C_{1-6}$ alkoxy, halogen, nitro, phenyl, benzyl, phenyloxy, benzyloxy,  $-C(=O)$ phenyl, amino, alkylamino, and aminoalkyl, wherein when  $R_{33}$  includes a phenyl group said phenyl group in turn is optionally substituted with one to two of halogen, nitro, cyano,  $C_{1-4}$  alkyl, and/or  $C_{1-4}$  alkoxy.

Claim 8. (Previously Presented) A compound according to claim 1 or a pharmaceutically-acceptable salt or hydrate thereof, in which

$R_2$  is selected from hydrogen,  $C_{1-6}$ alkyl,  $C_{2-6}$ alkenyl, biphenyl,  $C_{2-6}$ alkenylene-K, and  $-(CH_2)_g$ -K;

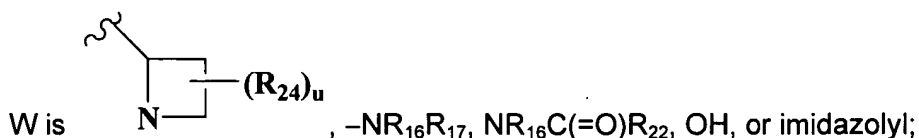
K is selected from phenyl, naphthyl, thienyl, thiazolyl, pyridinyl, pyrimidinyl, and  $C_{5-6}$ cycloalkyl, wherein each group K in turn is optionally substituted with one to three  $R_{30}$  or has a benzene ring fused thereto, which also may be substituted with one to three  $R_{30}$ ;

$R_{30}$  is selected from  $C_{1-4}$ alkyl, hydroxy, alkoxy, halogen, nitro, cyano, amino, alkylamino, phenyl, and acylphenyl; and

$g$  is 0, 1, 2 or 3.

Claims 9 and 10. (Cancelled).

Claim 11. (Previously Presented) A compound according to claim 1, or a pharmaceutically-acceptable salt or hydrate thereof, in which



$R_{16}$  and  $R_{17}$  are selected from hydrogen and  $C_{1-4}$ alkyl;

$R_{22}$  is  $C_{1-4}$ alkyl, phenyl or piperidinyl $C_{1-4}$ alkyl;

$R_{24}$  is  $C_{1-4}$ alkyl; and

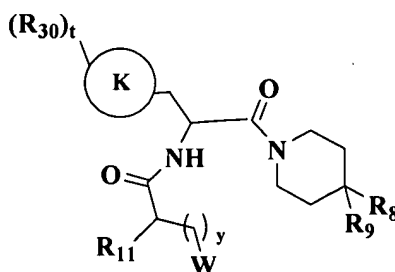
$u$  is 0 or 1.

Claim 12. (Previously Presented) A compound according to claim 11, or a pharmaceutically-acceptable salt or hydrate thereof, in which

$R_{11}$  is hydrogen,  $C_{1-4}$ alkyl, or imidazolyl $C_{1-4}$ alkyl.

Claim 13. (Previously Presented) A compound according to claim 11 or a pharmaceutically-acceptable salt or hydrate thereof, in which  $R_{16}$  and  $R_{17}$  are independently selected from hydrogen,  $C_{1-8}$ alkyl, and  $C_{1-8}$ substituted alkyl, except  $R_{16}$  and  $R_{17}$  are not alkyl substituted with pyridyl, imidazolyl, thiazolyl, pyrimidinyl, or piperazinyl, and W is not morpholinyl.

Claim 14. (Currently Amended) A compound according to the formula,



or a pharmaceutically-acceptable salt or hydrate thereof, in which,

K is aryl or heteroaryl;



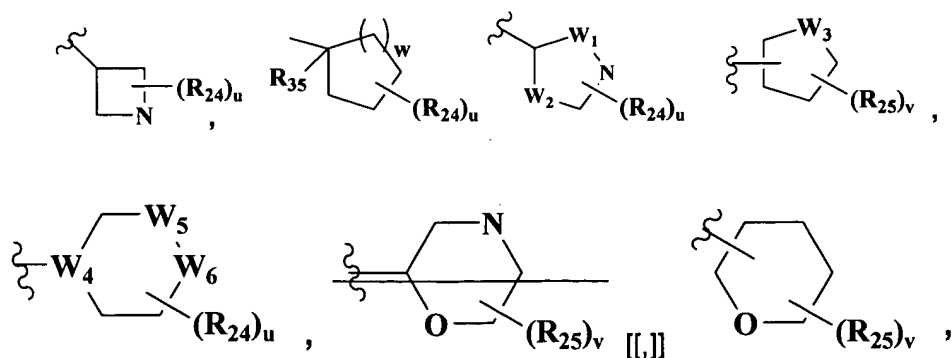
$R_8$  and  $R_9$  are independently alkyl substituted with heteroaryl, cycloalkyl, aryl, and,  $-C(=O)R_{13}$ ;

$R_{11}$  is selected from hydrogen, alkyl, halogen, hydroxy, hydroxyalkyl, haloalkyl, amino, aminoalkyl, alkylamino, arylalkyl, cycloalkylalkyl, heteroarylalkyl, aryl, and cycloalkyl, and where  $y$  is at least 1, then  $R_{11}$  and  $R_{12}$  may be heterocyclo or heterocycloalkyl;

$R_{13}$ ,  $R_{14}$  and  $R_{15}$  are independently is hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heterocyclo, or heteroaryl; or  $R_{13}$  and  $R_{14}$ , or  $R_{14}$  and  $R_{15}$ , may join together to form a heterocyclo or heteroaryl, except  $R_{14}$  is not hydrogen when joined to a sulfonyl group as in  $-S(O)_pR_{14}$  or  $-NR_{13}SO_2R_{14}$ ;

W is selected from:

- 1)  $-NR_{16}R_{17}$ ,  $-NR_{16}C(=O)R_{22}$ ,  $-NR_{16}CO_2R_{22}$ , or  $-OR_{23}$ ; or
- 2) heteroaryl or heterocyclo groups selected from pyrrolyl, furyl, thienyl, imidazolyl, pyrazolyl, isoxazolyl, thiazolyl, isothiazolyl, 3-azaisothiazolyl, pyridyl, pyrazinyl, pyridazinyl, 1,2-dihydropyridazinyl, and pyranyl, wherein said heteroaryl and heterocyclo groups may be optionally substituted with one to three  $R_{36}$ , and may have an optionally-substituted carbocyclic, heterocyclic or heteraryl ring fused thereto; or
- 3) a carbocyclic, heterocyclic, or heteroaryl ring selected from:



in which  $W_1$  and  $W_2$  are NH,  $CH_2$ , O or S,  $W_3$  is O or S,  $W_4$  is N or CH, and  $W_5$  and  $W_6$  are NH or  $CH_2$ , wherein when  $W_1$ ,  $W_2$ ,  $W_5$  and  $W_6$  are NH or  $CH_2$ , said groups are optionally substituted with  $R_{24}$ ;

$R_{16}$  and  $R_{17}$  are  $C_{1-8}$ alkyl or  $(CH_2)_q$ -J, wherein J is selected from aryl, heteroaryl, heterocyclo, and cycloalkyl, wherein the alkyl, alkylene, and/or J groups of  $R_{16}$  and/or  $R_{17}$  are optionally substituted with up to three  $R_{32}$ ;

$R_{22}$  is selected from  $C_{1-6}$ alkyl, trifluoromethyl, alkoxyalkyl, furylalkyl, alkylaminoethyl, phenyl, pyrrolylalkyl, piperidiny, and piperidinylalkyl, wherein  $R_{22}$  in turn is optionally substituted with one to two  $C_{1-4}$ alkyl and/or  $-CO_2(C_{1-4}alkyl)$ ;

$R_{23}$  is hydrogen or aryl;

$R_{24}$  and  $R_{25}$  at each occurrence are attached to any available carbon or nitrogen atom of W and at each occurrence are selected from hydrogen,  $C_{1-6}$ alkyl, halogen, substituted  $C_{1-6}$ alkyl, amino, alkylamino,  $-C(=O)R_{26}$ ,  $-CO_2R_{26}$ ,  $-SO_2R_{26}$ ,  $-OR_{26}$ , aryl, heteroaryl, heterocyclo, and cycloalkyl, and/or two  $R_{25}$  attached to two adjacent carbon atoms or adjacent carbon and nitrogen atoms may be taken together to form a fused optionally-substituted heteroaryl, heterocyclo or cycloalkyl ring, and/or two  $R_{24}$  or two  $R_{25}$  when attached to the same carbon atom may form keto ( $=O$ );

$R_{26}$  is hydrogen, alkyl, phenyl, benzyl, or aminoalkyl, except when joined to a sulphonyl group as in  $SO_2R_{26}$ , then  $R_{26}$  is not hydrogen;

$R_{32}$  is selected from  $C_{1-6}$ alkyl, hydroxy,  $C_{1-6}$ alkoxy, halogen, nitro, phenyl, benzyl, phenyloxy, benzyloxy,  $-C(=O)phenyl$ , amino, alkylamino, and aminoalkyl, wherein when  $R_{32}$  includes a phenyl group said phenyl group in turn is optionally substituted with one to two of halogen, nitro, cyano,  $C_{1-4}$  alkyl, and/or  $C_{1-4}$  alkoxy;

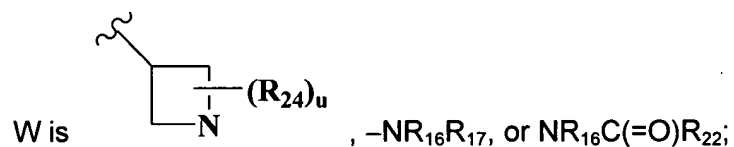
$R_{35}$  and  $R_{36}$  at each occurrence is selected from  $C_{1-6}$ alkyl, halogen, substituted  $C_{1-6}$ alkyl, hydroxy, alkoxy, cyano, trifluoromethyl, trifluoromethoxy, nitro, acyl, carboxyalkyl, sulfonyl, aryl, heteroaryl, heterocyclo, and cycloalkyl;

$p$  is 1, 2 and 3;

$u$  and  $v$  are 0, 1, or 2; and

w is 0, 1, or 2.

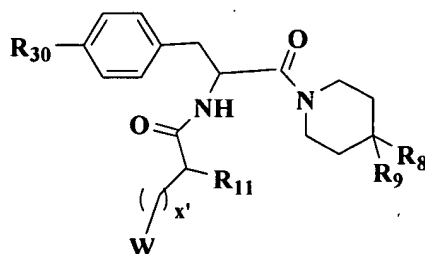
Claim 15. (Previously Presented) A compound according to claim 14, or a pharmaceutically-acceptable salt or hydrate thereof, in which



$\text{R}_{24}$  is  $\text{C}_{1-4}$ alkyl;

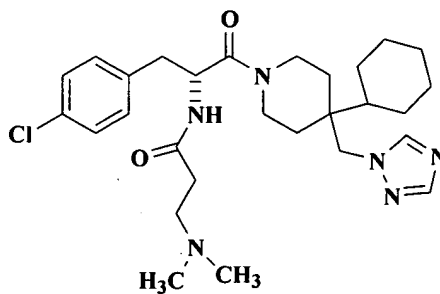
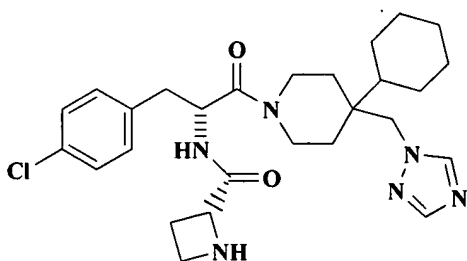
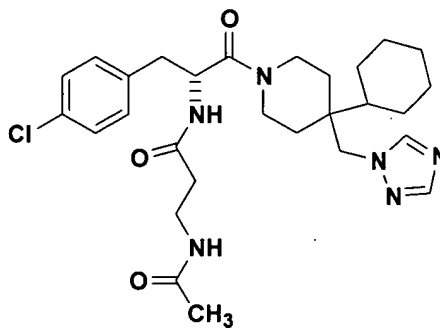
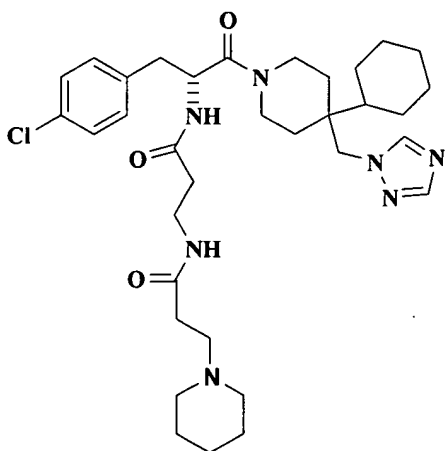
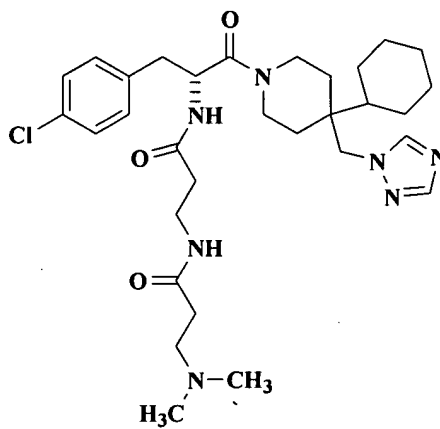
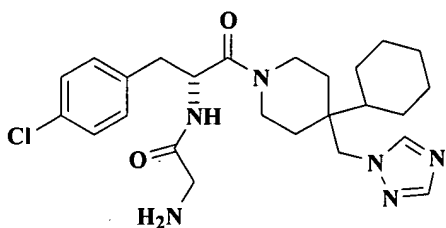
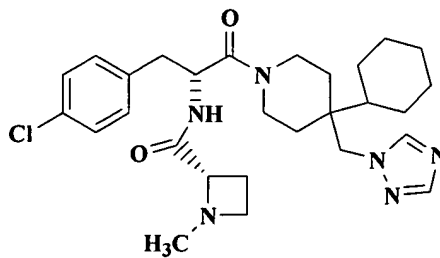
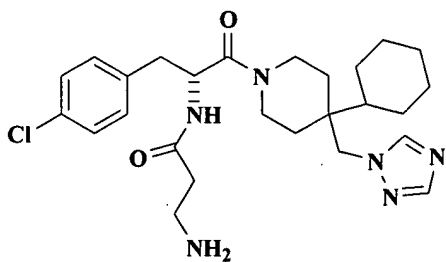
$u$  is 0 or 1.

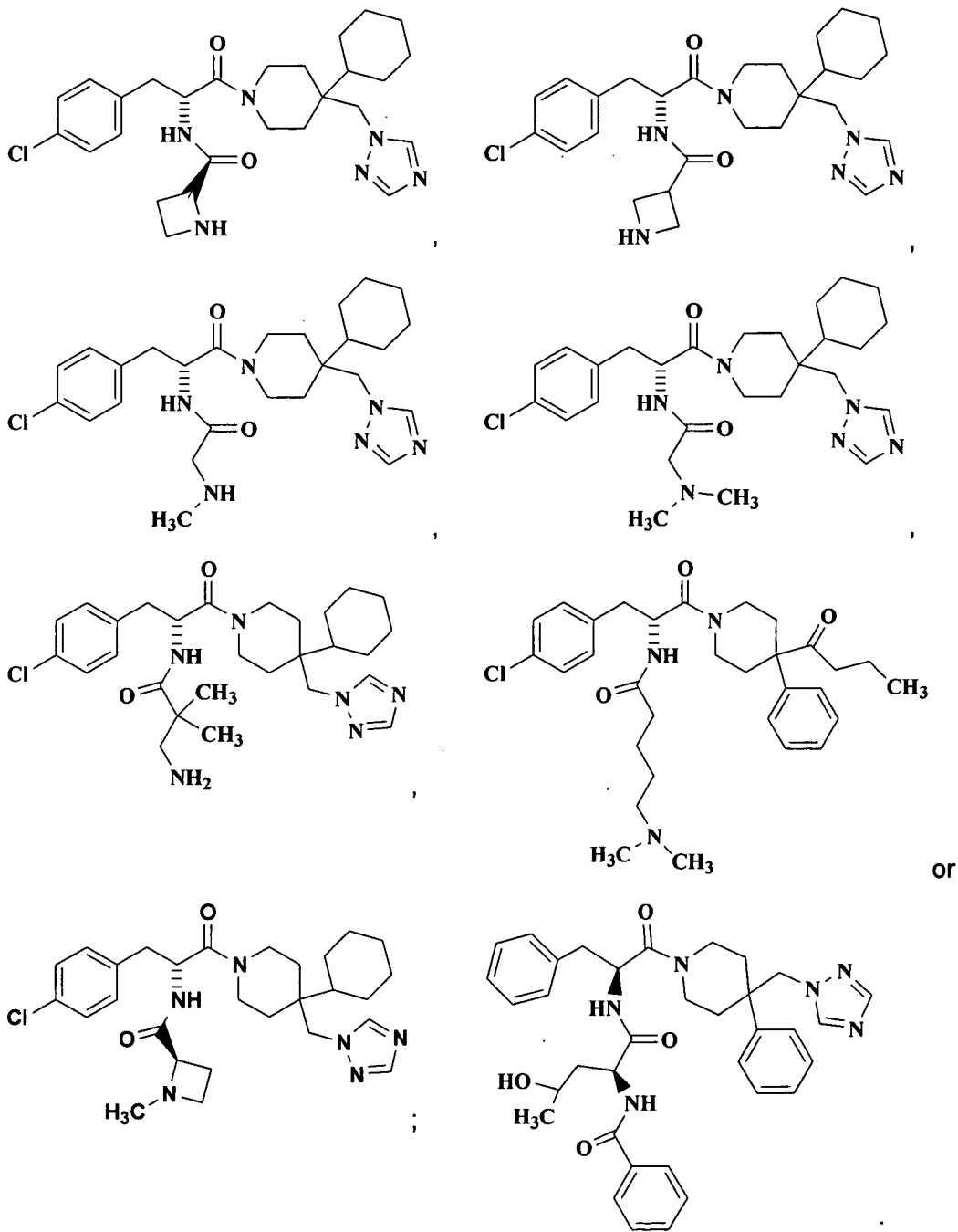
Claim 16. (Previously Presented) A compound according to claim 14, or a pharmaceutically-acceptable salt or hydrate thereof, having the formula,



in which  $y$  is 0, 1 or 2 and  $\text{R}_{30}$  is halogen or methoxy.

Claim 17. (Previously Presented) A compound having the formula,





or a pharmaceutically-acceptable salt, hydrate, or prodrug thereof.

Claim 18. (Previously Presented) A pharmaceutical composition comprising a therapeutically effective amount of at least one compound according to claim 1 or a

pharmaceutically-acceptable salt, hydrate or prodrug thereof; and a pharmaceutically-acceptable carrier or diluent.

Claim 19. (Original) A pharmaceutical composition comprising (i) at least one compound according to claim 1 or a pharmaceutically-acceptable salt, hydrate or prodrug thereof, (ii) at least one second compound effective for treating an inflammatory or immune disease, a cardiovascular disease, or neurodegenerative disorder; and (iii) a pharmaceutically-acceptable carrier or diluent.

Claim 20. (Original) The pharmaceutical composition according to claim 19 in which the at least one second compound comprises a phosphodiesterase inhibitor.

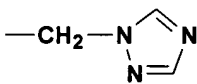
Claim 21. (Currently Amended) A method of treating a disease or disorder treatable by a melanocortin-receptor agonism which are neurodegenerative disorders, inflammatory or immune diseases, sexual dysfunction, cardiovascular diseases, skin conditions, body weight disorders or cancer which are inflammatory bowel disease, irritable bowel syndrome, gall bladder disease, Crohn's disease, rheumatoid arthritis, osteoarthritis, osteoporosis, traumatic arthritis, rubella arthritis, muscle degeneration, pancreatitis (acute or chronic), psoriasis, glomerulonephritis, serum sickness, lupus (systemic lupus erythematosus), urticaria, scleraclerma, schleroderma, chronic thyroiditis, Grave's disease, dermatitis (contact or atopic), dermatomyositis, alopecia, atopic eczemas, ichthyosis, fever, sepsis, migraine, cluster headaches, Alzheimer's Disease, Parkinson's disease, Creutzfeldt-Jacob disease, multiple sclerosis, tuberculosis, dementia, and transplant or graft-host rejections, asthma, acute respiratory distress syndrome, hayfever, allergic rhinitis, and chronic obstructive pulmonary disease; and inflammatory disorders of the central nervous system, HIV encephalitis, cerebral malaria, meningitis, and ataxia telangiectasis, post-operative pain, neuromuscular pain, headache, pain caused by cancer, dental pain, and arthritis pain, herpes simplex type 1 (HSV-1), herpes simplex type 2 (HSV-2), cytomegalovirus, Epstein-Barr, human immunodeficiency virus (HIV), Addison's disease (autoimmune disease of the adrenal glands), idiopathic adrenal insufficiency, autoimmune polyglandular disease or syndrome, chronic active hepatitis or acute hepatitis infection, hepatitis A, hepatitis B, and hepatitis C, autoimmune gastritis, autoimmune hemolytic anemia, and autoimmune neutropenia, fungal infections, atherosclerosis, transplant atherosclerosis, peripheral vascular disease, inflammatory vascular disease, intermittent

claudication, restenosis, cerebrovascular stroke, transient ischemic attack, myocardial ischemia and myocardial infarction, hypertension, hyperlipidemia, coronary artery disease, unstable angina, thrombosis, thrombin-induced platelet aggregation, and/or consequences occurring from thrombosis and/or the formation of atherosclerotic plaques, traumatic brain injury, vitiligo, alopecia areata, photosensitivity disorders, albinism, and porphyria, depression, anxiety, compulsion (obsessive-compulsive disorder), neuroses, psychosis, insomnia/sleep disorder, sleep apnea, and drug or substance abuse, sexual dysfunction which is impotence, loss of libido, and erectile dysfunction, ejaculatory failure, premature ejaculation, or an inability to achieve or maintain an erection or inability to achieve an orgasm, sexual arousal disorder or disorders relating to desire, sexual receptivity, orgasm, and/or disturbances in trigger points of sexual function, sexual pain, premature labor, dysmenorrhea, excessive menstruation, and endometriosis, obesity and anorexia and diabetes mellitus, cancer of the lung, prostate, colon, breast, ovaries, and bone, or angiogenic disorders, formation or growth of solid tumors, comprising administering to a warm-blooded species in need of such treatment a melanocortin-receptor agonistic-effective amount of at least one compound according to claim 1.

Claim 22. (Currently Amended) The method of claim 21 in which the disease or disorder treatable by melanocortin-receptor agonism is an MC-1R or MC-4R associated condition which is an inflammatory or immune condition which is inflammatory bowel disease, irritable bowel syndrome, Crohn's disease, arthritis, HSV-1, HSV-2, HIV, Addison's disease, Epstein-Barr, autoimmune gastritis, autoimmune hemolytic anemia, and autoimmune neutropenia.

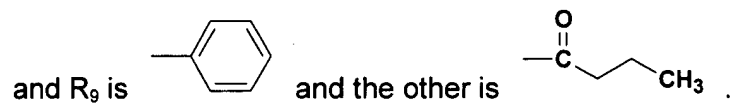
Claim 23. (Cancelled).

Claim 24. (Currently Amended) The compound as defined in Claim 23 1 wherein one of R<sub>8</sub>

and R<sub>9</sub> is  and the other is cyclohexyl.

Claim 25. (Cancelled).

Claim 26. (Currently Amended) The compound as defined in Claim 25 1 wherein one of R<sub>8</sub>



Claim 27. (Previously Presented) A compound having the structure

